Deckblatt Übersetzung

Daten der Übersetzung:

Court/Gericht:	Bundesgerichtshof
Date of Decision / Datum der Entscheidung:	2014-02-25
Docket Number / Aktenzeichen:	X ZB 6/13
Name of Decision / Name der Entscheidung:	Collagenase II

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– X ZB 6/13 –
German Patent Appln. 100 27 521.4-41

Your Ref.:
Our Ref.: E1631 DE PT/sh

English translation of the judgment issued by the Federal Court of Justice
on February 25, 2014

FEDERAL COURT OF JUSTICE

JUDGMENT

X ZB 6/13

of February 25, 2014

in the appeal proceedings

regarding the German Patent Application 100 27 521.4-41

Applicant and Appellant

– Counsel:

Reference book: yes
BGHZ: no
BGHR: yes

Collagenase II

PatG [German Patent Act] Section 4

a) The instruction to immobilize a body part for several hours immediately after the injection of a drug in order to prevent the drug from spreading to other body parts is not suggested by the prior art simply because of the fact that it was known at the priority date that complications occurring several days after the treatment could be treated by immobilization.

b) In the assessment of whether a specific use of a drug is based on inventive step, methods which were obvious to the person skilled in the art because they were part of the standard medical repertoire at the priority date have to be taken into account as well.

BGH [Federal Court of Justice], judgment of February 25, 2014 – X ZB 6/13 – Federal Patent Court

On February 25, 2014, the X. Civil Senate of the Federal Court of Justice presided over by Judge Prof. Dr. Meier-Beck, with Judges Dr. Grabinski, Dr. Bacher, and Hoffman and Judge Schuster

has found:

> Following the appeal on a point of law, the decision issued by the 14th Senate (Technical Board of Appeal) on February 8, 2013 is set aside. The matter is remanded to the Federal Patent Court for a new hearing and decision.

Grounds:

A. The appeal on a point of law is directed to the refusal of a patent application.

The application was filed on June 2, 2000, claiming a priority of June 3, 1999, and is directed to the use of collagenase for treating Peyronie's disease. The latest valid wording of claim 1 in the appeal proceedings reads as follows:

> Collagenase for use in treating an individual suffering from Peyronie's disease wherein the collagenase is adapted for injection into a fibrous Peyronie's plaque in the penis of said individual in a pharmaceutically acceptable carrier substance in a total amount of at least about 20,000 ABC units in a concentration of about 20,000 to about 40,000 ABC units per ml carrier substance and for immobilizing the penis immediately after injection for several hours.

The Patent Office refused the application on the grounds that the subject matter of the claim is not based on an inventive step. Applicant's appeal – whose main request was directed to a version without the feature of immobilizing the penis – was unsuccessful. It is against that decision that the Applicant filed an appeal on a point of law allowed for by the Patent Court, maintaining the auxiliary requests submitted in the appeal instance.

B. The appeal on a point of law, which is allowable as a legal remedy and also

otherwise admissible, results in the decision under appeal being set aside and the matter being remanded to the Federal Patent Court.

I. The application is directed to a purpose-limited substance protection for collagenase for the treatment of Peyronie's disease.

1. According to the statements in the application, Peyronie's disease is an idiopathic condition (i.e. a condition having no known cause) resulting in penile deformity and disability as the result of scarring and contracture within certain connective tissue. The application lists several prior art documents relating to the treatment of this disease by injecting collagenase into the affected connective tissue.

The application does not specifically state which technical problem is addressed by the invention. It can be inferred from the description that the invention is directed to providing an improved use of collagenase for treating Peyronie's disease.

2. For solving this problem, the application suggests collagenase according to the primarily sought wording of claim 1 in the appeal proceedings, for a use whose features can be structured as follows:

0. The use is for treating Peyronie's disease.

1. The collagenase is injected into a fibrous Peyronie's plaque in the penis of an individual

2. in a pharmaceutically acceptable carrier substance.

3. The total amount injected is at least about 20,000 ABC units.

4. The concentration is about 20,000 to about 40,000 ABC units per ml carrier substance.

5. Immediately after injection, the penis is immobilized for several hours.

II. In as far as it is of interest for the appeal on a point of law, the Federal Patent Court essentially substantiated their decision as follows:

The subject matter of claim 1 is suggested by the prior art.

Feature 5, according to which the penis is to be immobilized immediately after injection must not be taken into account in the assessment of patentability. This feature is not an element of the preparation of a substance for use in the treatment of a disease. It does not serve to characterize the claimed collagenase or the formulation intended for administration. Rather, it is a mere instruction for the attending physician and thus relates to a therapeutic process which is excluded from patent protection. The previous decisions of the Enlarged Board of Appeal of the European Patent Office and the case law of the British courts do not suggest otherwise. The relevant decisions relate to novel dosage instructions. They are not comparable to the constellation to be evaluated here.

Independently, the subject matter of claim 1 is not even based on an inventive step if feature 5 is taken into account. The immobilization of the penis was suggested to the person skilled in the art by the publication of Gelbard et al. (*The use of collagenase in the treatment of Peyronie's disease*, J. Urol. 134 (1985), 280-283, D3).

III. This substantiation cannot withstand legal review.

1. Contrary to the opinion of the Federal Patent Court, feature 5 has to be taken into account in the examination of whether the subject matter of the application is patentable.

a) As the Patent Court correctly stated, patent protection can be sought for a substance for treating a disease – be it in the form of a use claim, be it in the form of a claim directed to purpose-limited substance protection according to Section 3 Subsection 4 PatG in the version in force since December 13, 2007 – even if the use for which the protection is sought only differs from the uses known in the prior art in a different dosage regimen.

aa) The Senate has repeatedly decided that patent protection for these

constellations is possible if the patent claim provides that the drug is adapted for use in the dosage in question (BGH, decision of December 19, 2006 – X ZR 236/01, BGHZ 170, 215 = GRUR 2007, 404 Ann. 51 – *Carvedilol II*; decision of September 24, 2013 – X ZR 40/12, GRUR 2014, 54 Ann. 34 – *Fettsäuren*).

The subject matter of such a patent claim is the suitability of a known substance for a specific medical use and thus ultimately a property inherent to the substance (BGH, decision of October 5, 2005 – X ZB 7/03, BGHZ 164, 220, 222 = GRUR 2006, 135, Ann. 11 – *Arzneimittelgebrauchsmuster*). In fact, this corresponds to purpose-limited substance protection as it is now explicitly provided in Section 3 Subsection 4 PatG and Art. 54(5) EPC for further indications. This applies independently of whether the wording of the patent claim is directed to the use of the drug, its preparation for a certain purpose, or – which in view of the new legal provision will probably be most expedient in the future – explicitly to purpose-limited substance protection.

bb) This is consistent with the previous decisions of the European Patent Office and the case law in other contracting states of the European Patent Convention.

According to the previous decisions of the European Patent Office, the medical use of a substance or substance mixture was even patentable according to the version of the European Patent Convention in force prior to December 12, 2007 if the new use is not the treatment of a different disease. The stipulation of Art. 54(5) EPC in force since December 13, 2007 – which, concerning its contents, corresponds to Section 3 Subsection 4 PatG – only changed this fact in that such uses now exclusively have to be purpose-limited substance claims instead of the previously mandatory claims worded in the Swiss format (decision of the Enlarged Board of Appeal of February 19, 2010 – G 2/08, OJ 2010, 456 Ann. 5.10.7 et seq. – *Dosierungsanleitung*/Abbott Respiratory with further references). According to both versions of the Patent Convention, patent protection is not excluded, either, if the only feature not included in the prior art is a dosage regimen (*loc. cit.* Ann. 6.1 et seqq.). The Court of Appeal for England and Wales (Actavis UK Limited v. Merck & Co. Inc., [2008] EWCA Civ 444 Ann. 44 et seqq.) and the Swiss *Bundesgericht* (Federal

Supreme Court of Switzerland) (decision of March 4, 2011 – 4A_435/2010, GRUR Int. 2012, 183, 186 et seq.) take the same view.

Both the Enlarged Board of Appeal and the Court of Appeal have reached the correct conclusion that the decision "*Carvedilol II*" does not contain anything to the contrary. The concerns expressed therein only refer to claims wordings which are directed to a pure dosage regimen completely removed from the adaptation for use of the substance. Whether these concerns should be taken into account in view of the legal provisions in force since December 13, 2007 is irrelevant in the present context. In any case, they are irrelevant if the claim is directed to a purpose-limited substance protection in the sense of Art. 54(5) EPC or Section 3 Subsection 4 PatG. This also applies independently of whether the wording of the claim is directed to the use of the drug, its preparation, or the protection of a substance for a limited use.

b) The same applies to instructions which do not relate to the dosage regimen but to other modalities of the claimed use.

aa) The Enlarged Board of Appeal has decided that a specific use (*eine spezifische Anwendung, toute utilization spécifique*) in the sense of Art. 54(5) EPC in the version in force since December 13, 2007 does not have to constitute the treatment of a different disease.

The revised version of the regulation was essentially designed to anchor the previous decision-making practice of the European Patent Office in the Patent Convention (EPO, OJ 2010, 456 Ann. 5.10.3 et seq. – *Dosierungsanleitung*/Abbott Respiratory). According to previous decisions of the European Patent Office, patent protection cannot only be sought for uses for treatment of a different disease or with a different dosage regimen. Rather, it is sufficient if the use differs from the uses known in the prior art – i.e. if it is novel – and if it is based on an inventive step. For this reason, patent protection was for example granted if the use related to a new group of patients to be treated, a new method of administration or another technical effect (*loc. cit.* Ann. 5.10.7 with further references).

bb) The same applies to the German patent law.

In this respect, the wording of Section 3 PatG corresponds to the wording of Art. 54 EPC. In 2007, it was adapted to the revised version of the Patent Convention in order to maintain the parallelism of European and national law (BT public. 16/4382, page 11). In view of this alone, it is out of the question that patentability should be evaluated differently according to German law than according to the Patent Convention.

In the Senate's view, the interpretation of Art. 54(5) EPC underlying the established case law of the European Patent Office is correct. The new version of the regulation does not make the grant of purpose-limited substance claims conditional on whether the protection sought is directed to a disease whose treatment with the substance at issue was not known in the prior art. Rather, a patent can be granted on any specific use of a substance in a process for the surgical or therapeutic treatment of the human or animal body if it is novel and inventive. The legal situation prior to December 13, 2007 was no different in this respect. As was already stated, the insertion of Art. 54(5) EPC and Section 3 Subsection 4 PatG was not intended to modify but rather to codify this situation.

Limitations to certain aspects of the use – for example to the dosage – are excluded by the very wording of the mentioned regulations. It would not be possible to reconcile them with the intents and purposes of these regulations anyway. The specific use of a substance for the therapeutic treatment is not only defined by the disease to be treated and the dosage. Rather, depending on the circumstances of the individual case, the method of administration (for example, orally, transdermally, or by way of different kinds of injections), the consistency of the substance (solid, liquid, gaseous), the patient group, or other parameters are relevant as well. All these parameters have in common that they influence the effect of the substance, i.e. that they can be of essential significance for achieving the desired success of the use. In any event, if a use not known in the prior art nor suggested to the person skilled in the art offers the prospect of improving the effects of the substance or of bringing about these effects under conditions previously considered

impossible, it is the goal of the law to grant patent protection, as long as the other requirements for patentability are met as well.

cc) No different assessment can be inferred from Section 2a Subsection 1 No. 2 PatG and Art. 53(c) EPC.

According to these regulations, patents shall not be granted for processes for the treatment of humans or animals by surgery or therapy. Even in accordance with the established case law of the Senate regarding the previous version of the law, this did not exclude the grant of patents for the use of a chemical substance for therapeutic purposes and thus their obvious adaptation for use in such a process (basic ruling, BGH, decision of September 20, 1983 – X ZB 4/83, BGHZ 88, 209, 216 et seqq. = GRUR 1983, 729, 730 et seqq. – *Hydropyridin*). The same has to apply according to the current version of the law which explicitly provides for a limited substance protection for such inventions.

Under this aspect as well, patentability cannot depend on whether the use for which protection is sought is directed to a disease which has previously not been treated with the substance or to the dosage regimen. Just like all other aspects of the effect of the substance, the treatment of a patient with a certain drug and its dosage are an integral part of the physician's activity. If the exclusion from patentability referring to this activity does not contradict the patentability of this substance limited to certain uses, this has to, in principle, apply to all the aspects of said use.

However, according to Section 2a Subsection 1 No. 2 PatG and Art. 53(c) EPC, the assessment of patentability must not take into account those aspects of the use which are not related to the properties of the substance for which protection is sought, and to its effect on the human or animal body. Therefore, instructions regarding therapeutic treatment can only contribute to patentability if they objectively aim at allowing, reinforcing, accelerating or otherwise improving the effect of the substance, but not if they relate to therapeutic measures which are additionally suitable, independently of the effects of the substance, for treating the disease at issue.

c) In the present constellation to be evaluated, the use to which the desired purpose-limited substance protection refers shows the required connection with the effect of the substance.

According to the explanations in the application, the immobilization of the penis for several hours immediately after injection according to feature 5 serves the purpose of avoiding any extravasation of the collagenase (column 3, lines 61 to 64). This corresponds to the statements of the Federal Patent Court.

Thus, the immobilization of the penis is not only an additional measure for treating Peyronie's disease independent of the effects of the collagenase. Rather, the measure is intended to improve the effect of the administered substance. Thus, it relates to the way the substance is used and therefore to an aspect which – regardless of the exclusion from patentability according to Section 2a Subsection 1 No. 2 PatG and Art. 53(c) EPC – has to be taken into account in the assessment of patentability

Contrary to the view of the Federal Patent Court, instructions which chemically or physically characterize the formulation intended for administration are not the only ones which should be considered. A dosage instruction does not necessarily influence the chemical or physical composition of the substance, either. It can, as was initially realized by the Federal Patent Court as well, be limited to the information that the drug should be administered at a certain dosage. The same applies analogously with respect to the method of administration. For instance, the instruction to administer the substance orally or transdermally may require certain types of dosage forms. However, as far as the protected use is concerned, the limited substance protection also refers to those dosage forms which can be administered in different ways. This also applies to the usage instructions at issue – injection immediately followed by immobilizing the penis for several hours.

2. The Federal Patent Court's alternative contemplation that the subject matter of claim 1 is not based on an inventive step even if feature 5 is taken into account cannot

withstand legal review, either.

a) However, without any error of law, the Federal Patent Court arrived at the conclusion that the prior art suggested to the person skilled in the art, a team including at least a urologist engaged in research and a pharmacist specialized in the technical field of pharmaceutical technology, the use of collagenase for the treatment of Peyronie's disease in a dosage of at least 20,000 ABC units as claimed in feature 3.

aa) According to the Federal Patent Court's findings, at the priority date the publication of Gelbard et al. from the year 1985 (D3) taught the person skilled in the art that collagenase is suitable for the treatment of Peyronie's disease and that no undesired side effects occur even if the dosage is increased to 4,850 units.

These statements withstand the attacks in the appeal on a point of law.

(1) The appeal on a point of law claims that a medical professional will take a critical look at the optimistic and grandiose statements made in a first publication regarding a new active ingredient, and will examine the entire contents of the paper for internal contradictions and statements which are inconsistent with the authors' assessments.

Contrary to the appeal on a point of law, this does not constitute an error of law.

The Federal Patent Court did not exclusively base the acknowledgement of D3 on the statements made therein by its authors. The court dealt with the results disclosed in D3 of the study described therein and reached the conclusion that the relatively high ratio of patients who showed significant improvement and the generally good tolerability of the active ingredient even at higher doses supported the optimistic assessment of the authors and their suggestion to carry out further tests with repeated and increased dosages. The court furthermore took into account that this assessment was essentially confirmed in the publication D2 which was published seven years later by the same authors. In view of the above, the Federal Patent Court was in a position to infer the disclosure content they based

their assessment on from reference D3 without committing an error of law.

(2) The appeal on a point of law refers to Applicant's submissions according to which D3 reports several instances of hypersensitivity reactions which cannot be attributed to the excipient ß-aminopropionile, and criticizes that the Federal Patent Court had played down the resulting risks.

This cannot call into question the actual findings of the Federal Patent Court, either.

The Federal Patent Court has addressed the hypersensitivity reactions documented in D3 and has reached the conclusion that this observation does not indicate that the administration of collagenase entails severe side effects. The court considered it decisive that, contrary to Applicant's submissions, the observed reaction did not occur in the patient who was given the highest dose and that this reaction could also be due to a combination of collagenase and ß-aminopropionitrile fumarate. This assessment is possible and is not called into question by the objection raised in the appeal on a point of law.

(3) On this factual basis, the Federal Patent Court reached the conclusion, without committing an error of law, that at the priority date reference D3 conveyed reasonable chances of success for the treatment of Peyronie's disease to the person skilled in the art and that the person skilled in the art had motivation to take up the suggestion formulated in D3 and carry out further tests with higher doses as well. The fact that a relatively long period of time elapsed between the date of the publication and the priority date does not lead to a different assessment for the simple reason that the opinion expressed in D3 was confirmed seven years later in D2.

bb) According to the findings of the Federal Patent Court, the publication from the year 1993 (*Collagenase versus placebo in the treatment of Peyronie's disease: a double-blind study*, J. Urol. 149 (1993), 56-58, D2), also by Gelbard et al., provided the technical teaching to the person skilled in the art that collagenase in an amount of 14,000 units is well tolerated, but that this dose could still be too low for the treatment of severe cases.

This assessment also withstands the objections in the appeal on a point of law.

(1) The appeal on a point of law claims that the fact reported in D2 that in patients with severe symptoms even the highest dose of 14,000 units did not lead to significant therapeutic success, and the assessment expressed in D2 that in the case of massive contracture, even considerable volumes of enzymatic collagenolysis appear unable to cause clinically apparent improvement, clearly show the person skilled in the art that in severe cases no improvement can be expected even with high doses.

This argument in the appeal on a point of law does not illustrate an error of law.

The Federal Patent Court took the passages from reference D2 into account in their assessment. However, the court did not attach the same importance to them as postulated in the appeal. Rather, the court came to the conclusion that the indication also contained in D2 that the observed failure could be due to the presence of too much collagen substrate indicated that a further dosage increase could lead to success. This factual assessment is possible and is not called into question by the objections raised in the appeal on a point of law.

(2) Against this background, the Federal Patent Court arrived at their assessment, without committing an error of law, that in view of the publications D3 and D2 the person skilled in the art had reason to administer higher dosages of collagenase when treating especially severe cases of Peyronie's disease.

This is not contradicted by the fact that the expectations raised in D3 were not confirmed in D2 for especially severe cases of the disease. Rather, the assessment expressed in D2 that the absence of the desired effect could be due to the presence of too much collagen substrate leaves open the possibility of being able to cleave it with an even higher amount of collagenase. In any case, the person skilled in the art had motivation to carry out more testing in that direction because the tests in the other patient groups documented in D2

turned out to be successful and because no severe side effects occurred in D2, either.

b) Without committing an error of law, the Federal Patent Court furthermore came to the conclusion that the concentration on 20,000 to 40,000 ABC units per ml carrier substance claimed in feature 4 was also suggested in the prior art.

The appeal on a point of law claims that this concentration was not disclosed in the prior art.

This does not call into question the assessment carried out by the Federal Patent Court.

In this connection, the Federal Patent Court stated that the mentioned concentration was an inevitable result of the increase in dosage suggested by the prior art and what was a suitable volume to be injected from a practical point of view. In view of this fact situation, no specific example of the claimed concentration in the prior art was needed. The connection between dosage and concentration found by the Federal Patent Court motivated the person skilled in the art to increase the concentration as well based on the increase of the dosage suggested in D3 and D2, even without a specific example thereof in the prior art.

c) However, the Federal Patent Court did commit an error of law in reaching the conclusion that the immobilization of the penis for several hours immediately after injection according to feature 5 was also suggested to the person skilled in the art by the prior art.

aa) The Federal Patent Court assumed that the fact mentioned in D3 that undesired side effects occurred in one patient which were treated by bandaging the penis for immobilizing it (D3, page 282, third paragraph) shows that this measure was already being considered by the person skilled in the art. In view of this, and the fact that hemorrhages occurred in a number of further patients independently of the administered collagenase dose, which was also documented in D3 (Table on page 281), the immobilization of the penis was obvious as a mere precautionary measure when considerably higher amounts of active ingredient were administered.

This conclusion is not legally accurate.

The side effects in a single patient documented in D3 occurred two weeks after the treatment. In view of this background, the only conclusion that can be drawn from the fact that the patient was treated by immobilizing the penis is that it is a common measure to treat or alleviate unspecified symptoms. It cannot be deduced that this measure also influences the effects of the collagenase and that it could therefore also be suggested as a measure supporting the desired effect or preventing side effects immediately after the administration of the drug, and not only as an after-treatment two weeks after the injection.

In view of this background, the fact that according to D3 hemorrhages occurred in other patients as well cannot support the conclusion drawn by the Federal Patent Court. In D3, the immobilization of the penis is only mentioned in one isolated case as a treatment of hemorrhaging which had already occurred. This does not indicate that the hemorrhaging occurring in other patients could have been prevented by a precautionary immobilization of the penis. D3 does not make such a connection, nor is it assumed that an immobilization of the penis would have been helpful for other patients suffering from hemorrhages. The Federal Patent Court failed to find other circumstances which could suggest such a conclusion.

bb) In contrast to the proceedings X ZB 5/13, the Federal Patent Court has not found that the immobilization of a body part after the local injection of a drug was a common measure the person skilled in the art was familiar with in order to locally limit the effects of the drug by way of established additional measures. As the matter is remanded to the appeal instance, Applicant will have the opportunity of commenting on this aspect in more detail as well. In this connection, the question could also arise whether the immobilization of a body part after the injection of collagenase in high dosages could have been suggested by the patent application underlying the case X ZB 5/13. That application was laid open before the priority date of the application at issue.

IV. In view of Section 109 Subsection 1 Sentence 1 PatG, no order for payment of costs is deemed appropriate. Applicant is the only party to the proceedings.

V. The Senate did not consider it necessary to schedule oral proceedings (Section 107 Subsection 1 Half-sentence 2 PatG).

Meier-Beck Grabinski Bacher

Hoffmann Schuster

Previous instance:
Federal Patent Court, decision of February 8, 2013 – 14 W(pat) 13/09 –